Cognitive Trajectories in Dementia: A Mixed-Effects ANOVA Study of MMSE Score Variations Over Time

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1.Introduction

The evaluation of cognitive function in patients with varying dementia statuses provides valuable insights into the progression and impact of this debilitating condition. In particular, the Mini-Mental State Examination (MMSE) is a widely recognized tool for assessing cognitive impairment. This research seeks to understand the cognitive trajectory of patients by analyzing MMSE scores obtained over successive visits. The overarching research question guiding this investigation is: How do MMSE scores vary across different dementia statuses, and do these variations interact significantly between two visits? To address this research question, a mixed-effects ANOVA will be employed.

2.Data Cleaning

The initial phase of the analysis involved careful data cleaning to ensure the reliability of the results. The dataset, titled "INF2178_A4_data.csv," required several cleaning procedures:

a. Redundant column (Unnamed:0) removal,
b. Handling missing values in "SES" and "MMSE" columns with each's mean,
c. Converting data types of "Group", "M/F", "Hand" to category.

3.Exploratory Data Analysis

The EDA phase of this report serves as the foundation for understanding the underlying patterns and distributions within this dataset, setting the stage for more complex statistical analyses.

a. What's the distribution of sex in each dementia group?
b. What's the distribution of MMSE scores by sex and visit times?
c. How do educational level (EDUC), socioeconomic status (SES), Mini-Mental State Examination (MMSE) scores, and Clinical Dementia Rating (CDR) scores vary across different dementia statuses (nondemented, demented, converted)?

A closer examination of our dataset reveals a compelling gender distribution across different dementia statuses, as shown in the bar chart figure 1. Within the "Demented" group, we observe a notable difference in gender count, possibly indicating a gender predilection towards dementia, while the "Nondemented" group exhibits a more skewed direction towards females. Females also exhibit more counts in the "Converted" group, which suggest that for dementia, males could be more likely to get. Also, according to the box plot figure 2, females' MMSE scores' median is comparably higher than males in both visits. On the other hand, the similar distribution shapes between genders across visits could indicate that the process of cognitive change over time in this sample is not profoundly influenced by gender. In addition, for both genders, the MMSE scores exhibit some variability between the first and the second visits. Notably, the range of scores, as represented by the interquartile range (IQR), appears consistent across visits for both genders, indicating stability in the central tendency of cognitive performance over time.

The series of boxplots as shown in figure 3 compare the distributions of educational level, socioeconomic status, MMSE scores, and CDR scores across different dementia statuses. For education level, Nondemented individuals display the highest median education levels, which may suggest a potential

protective factor of education against cognitive decline. For socioeconomic status, the demented group exhibits a higher median of SES than the other groups. As for MMSE scores, there is a clear differentiation in MMSE scores as expected. The demented group has a significantly lower median of MMSE scores.

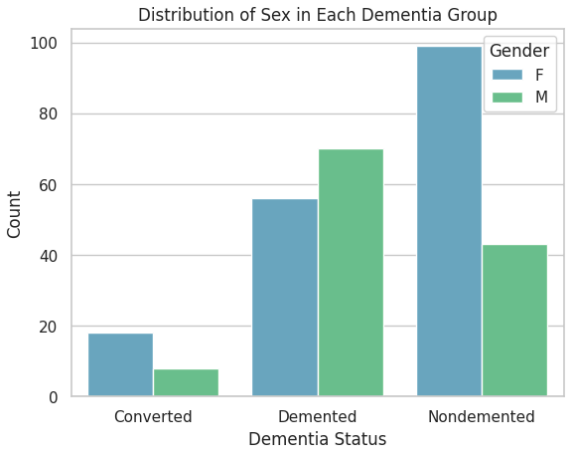

Figure 1.Distribution of Sex in Each Dementia Group

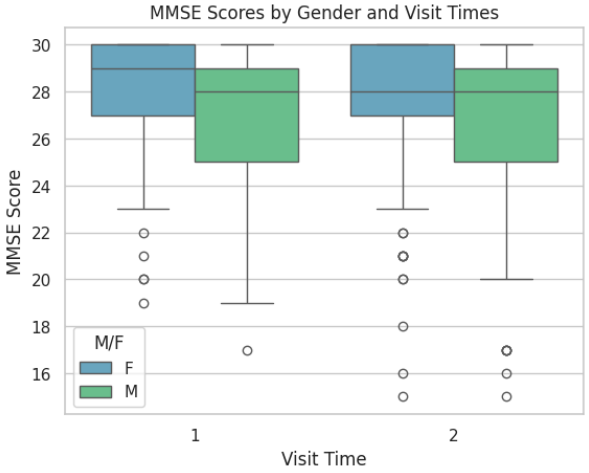

Figure 2. MMSE Scores by Gender and Visit Times

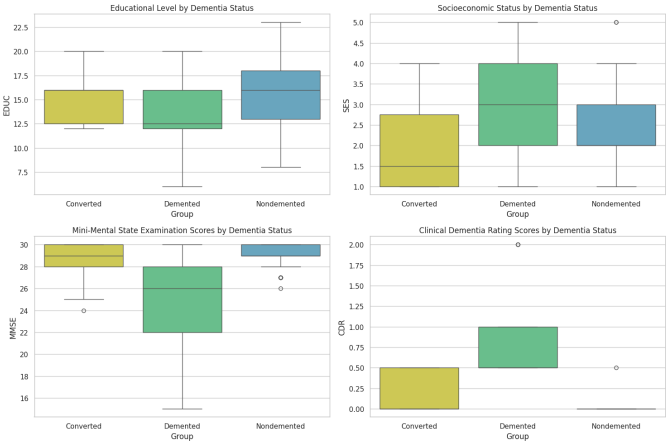

Figure 3. Differences in Educational, Socioeconomic, and Clinical Measures by Dementia Status

4.Mixed Effects ANOVA

By using mixed effects ANOVA, the hypothesis are:

- Null Hypothesis (H0): There is no significant difference in MMSE scores across the dementia statuses and no significant interaction effect between dementia status and the timing of visits on MMSE scores.
- Alternative Hypothesis (H1): There is a significant difference in MMSE scores across different dementia statuses and a significant interaction between dementia status and visit timing that affects MMSE scores.

The results of the mixed-effects ANOVA as shown in table 1 provides a comprehensive overview of the relationship between dementia status, visit time, and cognitive function as measured by MMSE. With an F-value of 56.100 and a p-value less than 0.001, the analysis shows a highly significant effect of dementia status on MMSE scores. The large effect size (np2 = 0.443) indicates a strong association; hence, the null

hypothesis can be rejected for the group effect. It's evident that dementia status has a significant impact on cognitive function as measured by MMSE. The visit time also has a significant effect on MMSE scores ($F = 8.525$, $p = 0.004$), suggesting that cognitive function varies from one visit to the next. This could reflect progression in the underlying dementia condition or the impact of other temporal factors. Finally, the interaction between dementia status and visit time has a p-value of 0.043, which is less than the conventional alpha level of 0.05, albeit with a small effect size ($np2 = 0.044$). This indicates a significant, although modest, interaction between dementia status and visit time on MMSE scores, suggesting that the trajectory of cognitive function over time differs among the dementia statuses.

	SS	DF1	DF2	MS	F	p-unc	np2	eps
Group	1322.017	2	141	661.009	56.100	<0.001	0.443	NaN
Visit	21.528	1	141	21.528	8.525	0.004	0.057	1.000
Interaction	16.204	2	141	8.102	3.208	0.043	0.044	NaN

Table 1. ANOVA Summary Table for the research question

Contrast	Visit	A	B	Paired	Parametric	T	dof	alternative	p-unc
Visit	-	1	2	True	True	2.876	143.000	two-sided	0.005
Group	-	Con	Dem	False	True	6.745	50.480	two-sided	<0.001
Group	-	Con	Nond	False	True	-1.303	12.315	two-sided	0.216
Group	-	Dem	Nond	False	True	-9.512	65.514	two-sided	<0.001
Visit * Group	1	Con	Dem	False	True	8.076	60.165	two-sided	<0.001
Visit * Group	1	Con	Nond	False	True	0.489	13.999	two-sided	0.633
Visit * Group	1	Dem	Nond	False	True	-9.124	68.185	two-sided	<0.001
Visit * Group	2	Con	Dem	False	True	4.515	33.372	two-sided	<0.001
Visit * Group	2	Con	Nond	False	True	-1.816	11.802	two-sided	0.095
Visit * Group	2	Dem	Nond	False	True	-8.480	66.145	two-sided	<0.001

Table 2. Post-hoc Test Result

The post-hoc test result as shown in table 2 provides a deeper exploration into the differences between specific groups identified as significant in the ANOVA. The MMSE scores significantly differ from the first to the second visit, indicating a possible progression or change in cognitive status over time. There is a significant difference in MMSE scores between converted and demented groups, as well as between demented and nondemented groups. This suggests distinct cognitive trajectories depending on the progression of dementia. Moreover, the interaction effects between visit times and dementia statuses are particularly telling. The significant interactions indicate that the change in MMSE scores from the first to the second visit is not uniform across all dementia statuses, highlighting a complex relationship between the progression of dementia and its impact on cognitive scores over time.

According to the interaction plot (figure 5), it seems that the trajectories of the nondemented and converted groups intersect. The MMSE scores for the nondemented group stay nearly the same across both visits, whereas the converted group, initially exhibiting higher MMSE scores, shows a notable

decline from the first to the second visit. From the output plot (figure 4), we can confirm that the demented group records the lowest MMSE scores at both visits.

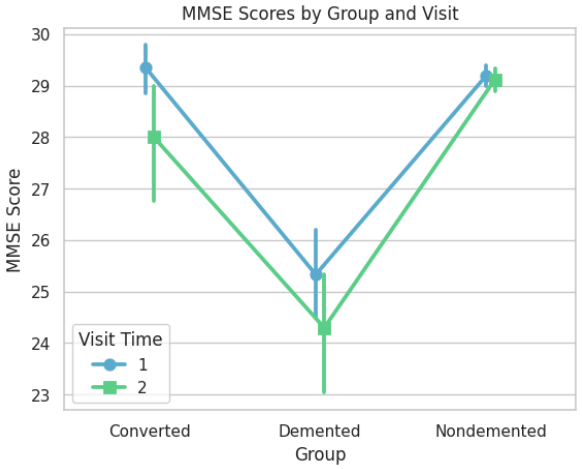

Figure 4.Output plot of the ANOVA

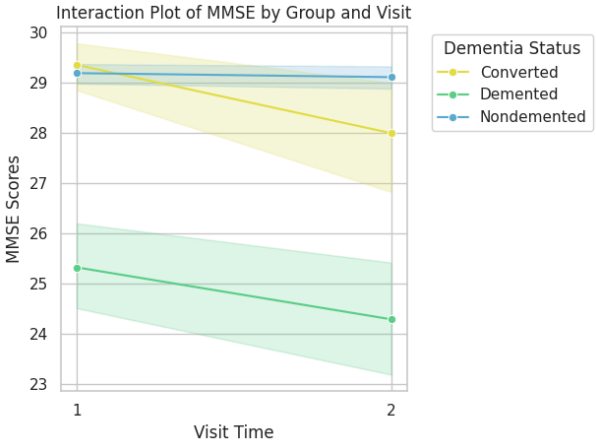

Figure 5.Interaction plot of MMSE

To check the assumptions, Shapiro-Wilk Test (table 3) and Levene's Test (table 4) are both conducted. For the assumption of normality of residuals, the extremely low p-values in both visits indicate that the residuals do not follow a normal distribution, which is a violation of one of the key assumptions of ANOVA. As for the homogeneity of variances, table 4 shows the rejection of the null hypothesis that variances are equal across groups, indicating that the group variances are not homogenous. These test results suggest that the statistical tests that assume normality of residuals and equal variances may not be entirely valid, and the results should be interpreted with caution.

	W	p-value	normal
Visit 1	0.787	1.761e-13	False
Visit 2	0.761	4.941e-13	False

Table 3. Shapiro-Wilk Test Result

	W	p-value	equal_var
Levene	64.643	5.897e-24	False

Table 4. Levene Test Result

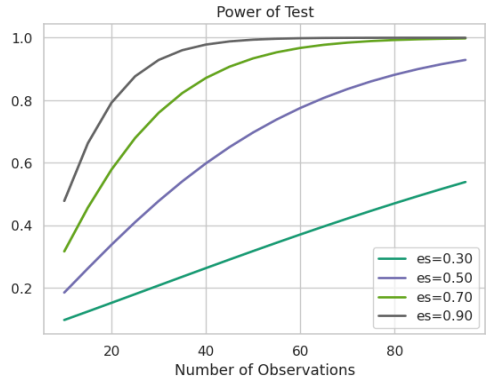

Figure 6. Power Curves

5.Statistical Power Analysis

The provided power curves graphically represent how the power of the test increases with an increasing number of observations for different effect sizes. As illustrated, with larger effect sizes, the power of the test increases, requiring fewer observations to achieve a high level of power. For example, to achieve a power of 0.91 with an effect size of 0.7, our analysis requires approximately 46 participants, as indicated by the calculation (45.451). This indicates that for a moderate to large effect, a sample size of about 45 is sufficient to detect a true effect with 91% probability while maintaining a 5% chance of a Type I error, where we incorrectly reject the null hypothesis.